REMARKS/ARGUMENTS

The claims have been amended to further define the present invention and expedite prosecution. Specifically, the claims are now directed toward oncomodulin for treatment of a neuronal injury. Support can be found throughout the specification, e.g., page 3, line 15 – page 6, line 21. No new matter has been added by the amendments to the claims.

Claims 1, 2, 6, 8 – 14, 35, and 37 stand rejected under 35 U.S.C. 112, first paragraph. The Examiner takes the position that while the specification is enabling for a method of comprising administering to a subject therapeutically effective amount of oncomodulin by introduction into a region of neuronal injury of retinal ganglion cells and producing an effect on neuronal survival, regeneration, and axonal outgrowth, it does not enable any person skilled in the art to use the invention commensurate in scope with the claim.

Applicant respectfully disagrees and request that this objection be withdrawn for the following reasons.

First, as noted above, in order to expedite prosecution Applicant has amended the claims to the elected species, oncomodulin. Applicant reserves the right to prosecute divisional/continuation applications directed to other macrophage-derived factors.

Secondly, the Examiner has alleged that the present disclosure fails to show that injection of oncomodulin directly causes neuronal protection effects.

Applicant directs the Examiner's attention to the attached declaration by Dr. Larry Benowitz (sometimes referred to as the "Benowitz Declaration"), inventor of the above-identified application, in which Dr. Benowitz sets forth experimental data showing that oncomodulin stimulates mature rat RGCs to regenerate their axons through an injured optic nerve crush *in vivo* is set forth. As illustrated in the figure attached to the declaration (Appendix

B), dBcAMP alone had no effect on growth, while oncomodulin plus dBcAMP caused many RGCs to regenerate their axons through the optic nerve (Benowitz declaration ¶ 4).

In light of the above and the amendments to the claims, Applicants respectfully requests that the rejection be withdrawn.

Claims 4, 5, 15 – 17, 29 – 31, 36, and 44 – 46 stand rejected under 35 U.S.C. 112, first paragraph. According to the Examiner, the specification does not enable the claimed invention. Specifically, the Examiner takes the position that the specification does not enable administration to a subject of a cAMP modulator.

Applicant respectfully disagrees and request that this rejection be withdrawn for the following reasons.

Applicant notes that the claims as amended are now directed to oncomodulin alone and in combination with a non-hydrolyzable cAMP analogue, e.g., dBcAMP, to provide neuronal survival, regeneration and axonal outgrowth. Applicant again kindly directs the Examiner's attention to the attached declaration by Dr. Benowitz. As noted in the declaration, the combination of oncomodulin plus dBcAMP, caused RGCs to regenerate their axons through the optic nerve (Benowitz Declaration ¶ 4).

Claims 15 and 17 are drawn to methods comprising different routes of administration. According to the Examiner, the present application is limited to a single interocular injection around the optic nerve via a posterior approach. The Examiner adds that there is no sufficient guidance or working example demonstrating that administering by any recited routes of administration would produce an effect on neuronal survival, regeneration or axonal outgrowth.

Applicant respectfully disagrees. It is clear when the specification is read as a whole, that the important aspect of the invention is contact between the oncomodulin and the neuronal injury. Applicant respectfully submits that the mode of administration is irrelevant as long as the

contact takes place. For example, while Applicant's exemplified the claimed invention using an interocular injection, Applicant has further shown in the attached declaration by Dr. Benowitz that implantation of polymeric beads releasing oncomodulin also stimulate RGCs to regenerate their axons (Benowitz Declaration ¶ ¶ 3 and 4).

With regard to claims 29 – 31 and 44 – 46, the Examiner has taken the position that the claims directed to methods of treating neurological disorders, such as spinal cord injury, are not enabled because Applicant only tested oncomodulin in culture. Applicants respectfully disagree.

As noted above, Applicant has attached hereto a declaration by Dr. Larry Benowitz in which Dr. Benowitz demonstrates, in an *in vivo* model, that oncomodulin can stimulate mature rat RGCs to regenerate their axons through an injured optic nerve crush. As noted by Dr. Benowitz, this model is a standard in the field for the treatment of neuronal injury (Benowitz Declaration ¶ 4). Accordingly, the rejection should be withdrawn.

Claims 1, 4 – 6, 8 – 31, 35, and 36 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

While Applicant respectfully disagrees, as noted above, in order to expedite prosecution, Applicant has amended the claims. The presently claimed invention is directed to treatment using oncomodulin. Applicant reserves the right to file divisional/continuation applications in the future directed to treatment using other macrophage-derived factors.

Claims 1, 2, 4 – 6, 8 – 31, and 35 – 37 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as invention.

Applicant respectfully submits that the amendments to the claims have obviated this rejection, which should therefore be withdrawn.

Claims 1, 9 – 12, 14, 18, 27, and 30, stand rejected under 35 U.S.C. 102(b) as being anticipated by Flanders et al., Prog. Neurobiolo. 54:71-85, 1998).

As noted by the Examiner, Flanders relates to TGF-β. The present claims are directed to oncomodulin, and thus, there can be no anticipation. Accordingly, the rejection should be withdrawn.

Claims 35 – 37 are objected to due to informalities. According to the Examiner, claim 35 is essentially the same as claim 6, claim 36 is essentially the same as claim 4, whereas claim 37 is essentially the same as claim 2.

Applicant respectfully submits that the cancellation of claims 35 – 37 has obviated this rejection.

Accordingly, Applicant respectfully requests that this objection be withdrawn.

In view of the above and foregoing, it is respectfully submitted that the claims now on file are believed to be in condition for allowance, and prompt and favorable action is earnestly solicited. Should there be any question concerning this response or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Applicant: Larry I. Benowitz
Serial No.: 09/872,347
Filed: 06/01/2001
Title: METHODS AND COMPOSITIONS FOR PRODUCING A NEUROSALUTARY EFFECT IN A SUBJECT

Examiner: L.I. Riuxiang
Group: 1646

Authorization is hereby given to the Commissioner to charge any deficient fees or to credit any overpayment to account no. 50-0850.

Date: 5/29/03

Respectfully submitted,

Customer No.: 26770

David S. Resnick (Reg. No. 34,235)
NIXON PEABODY LLP
101 Federal Street
Boston, MA 02110
(617) 345-6057